Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Blood 138 (2021) 4875–4877

63rd ASH Annual Meeting Abstracts

ONLINE PUBLICATION ONLY

722.ALLOGENEIC TRANSPLANTATION: ACUTE AND CHRONIC GVHD, IMMUNE RECONSTITUTION

Serological Response Following BNT162b2 Anti-Sars-Cov-2 mRNA Vaccination in Hematopoietic Stem Cell Transplantation Patients

Imma Attolico[1], Francesco Tarantini[2], Paola Carluccio[1], Claudia Schifone[2], Mario Delia[1], Vito Pier Gagliardi[1], Tommasina Perrone[1], Francesco Gaudio[1], Chiara Longo[1], Annamaria Giordano[1], Nicola Sgherza[1], Paola Curci[1], Rita Rizzi[2], Alessandra Ricco[1], Antonella Vita Russo Rossi[1], Francesco Albano[2], Angela Maria Vittoria Larocca[3], Luigi Vimercati[4], Silvio Tafuri[5], Pellegrino Musto[6]

[1] Hematology and Stem Cell Transplantation Unit, AOUC Policlinico, Bari, Italy
[2] Department of Emergency and Organ Transplantation, "Aldo Moro" University School of Medicine, Bari, Italy
[3] Hygiene Unit, AOUC Policlinico, Bari, Italy
[4] Interdisciplinary Department of Medicine, "Aldo Moro" University School of Medicine, Occupational Medicine Unit, AOUC Policlinico, Bari, Italy
[5] Section of Hygiene, Department of Biomedical Science and Human Oncology, University of Aldo Moro Medical School, Bari, Italy
[6] Department of Emergency and Organ Transplantation, "Aldo Moro" University School of Medicine, Hematology and Stem Cell Transplantation Unit, AOUC Policlinico, Bari, Italy

Abstract Patients with hematological malignancies (HM) undergoing hematopoietic stem cell transplantation (HSCT) have an increased vulnerability to SARS-Cov-2 (Sharma et al, Lancet Haematology 2020; Ljungman et al, Leukemia 2021), the reason why international guidelines strongly support the need for a protective vaccination for these subjects. The most relevant data currently available on the response to a complete anti-SARS-Cov-2 vaccination cycle in HM patients after HSCT refer to 314 patients reported in a Lithuanian national survey (Maneikis et al, Lancet Haematol 2021). In this study, the median titers of antibodies against SARS-Cov-2, determined 7-21 days after the second vaccination, were comparable to that of healthy controls (HC) in both autologous and allogeneic groups, with no patient found below the protective threshold of 50 arbitrary units (AU)/ml. Notably, the large majority of patients had received the transplant more than 1 year before vaccination.
In a prospective, cohort study, we compared 114 patients, who had received an autologous or allogeneic HSCT at least three months before the first dose of vaccination, to 107 HC, matched for age and sex. Study population and HC received two doses of BNT162b2 anti-SARS-Cov-2 mRNA vaccine on days 1 and 21, between April and May 2021. Serological tests were performed by a commercially available immunoassay for the quantitative determination of anti-spike IgG antibodies to SARS-Cov-2. The cut-off for defining responders was 50 or greater AU/ml. Patients and HC samples were collected four weeks after the second dose of the vaccine.
Table 1 reports the main clinical characteristics of patients and HC. Eighteen of 114 patients (16%) did not respond (24% in the allogeneic group, 6% in autologous recipients). Overall, median antibodies titers did not differ between HC and the entire cohort of transplanted patients, recipients of allogeneic HSCT, all patients responding to the vaccine or responders in the autologous subgroup (Figure 1A). All autologous HSCT recipients had significantly lower titers of antibodies than HC, while higher levels were found in responders who had received allogeneic HSCT (Figure 1A). Responders in the allogeneic subgroup showed antibodies titers significantly higher than responders in the autologous subgroup (Figure 1B).
We further stratified patients in three groups, according to the time elapsed from transplant to vaccination: G1:<1 year; G2:1-5 years; G3:>5 years. Higher antibodies titers were observed in HC compared to all transplanted patients in G1 (Figure 1C), including both allogeneic (Figure 1D) and autologous (Figure 1E) HSCT recipients. No differences emerged in G2 between HC and all patients (Figure 1C), allogeneic (Figure 1D) or autologous (Figure 1E) HSCT recipients. Finally, no differences were found in G3 when comparing HC with all patients (Figure 1C) or allogeneic recipients (Figure 1D), whereas patients in the autologous subgroup showed significantly lower titers than HC (Figure 1E).
Myeloma patients with controlled disease showed higher titers than patients with active disease (Figure 1F). According to median age, autologous HSCT recipients older than 57 years had significantly lower antibody levels than younger patients

(Figure 1G). Autologous vs allogeneic HSCT, age of all patients and of allogeneic HSCT recipients, sex, type of allogeneic HSCT, conditioning regimen, age and sex of donor, occurrence of GVHD, disease type and single vs double autologous HSCT did not significantly impact on antibody levels (data not shown). No relevant side effects were recorded after vaccination. With a median follow up of 12 weeks, no case of COVID19 occurred among vaccinated patients.
In our single center study, patients with a previous history of HSCT tolerated well BNT162b2 vaccine and mounted a potentially protective immune response in the majority of cases one month after two doses of vaccine. However, lack of response was not rare, especially in the allogeneic setting. The main factor associated with the quality of response was the time from HSCT, with lower responses within the first year from transplant and differences between autologous and allogeneic groups transplanted more than five years before vaccination. Here, a consolidated, complete immune reconstitution in allogeneic HSCT recipients, as well as age and a still active disease in the autologous setting, could have played opposite pivotal roles.

Disclosures Delia: *Gilead:* Consultancy; *Amgen:* Consultancy; *abbvie:* Consultancy; *Jazz pharmaceuticals:* Consultancy.

https://doi.org/10.1182/blood-2021-147542

	PATIENTS (N= 114)	HEALTHY CONTROLS (N=107)
SEX M/F	65/49	60/47
MEDIAN AGE (RANGE)	56 (20-71)	53 (19-69)
RESPONSE TO VACCINATION RESPONDERS/NOT RESPONDERS (%)	96/18 (84,2/15,8)	107/0 (100/0)
ANTIBODY TITER (AU/mL) MEDIAN (RANGE)	4480 (0-104689)	7131 (216-67282)

	ALLO-HSCT (N=62)	AUTO-HSCT (N=52)
SEX M/F	33/29	32/20
MEDIAN AGE (RANGE)	56 (28-70)	57 (20-71)
RESPONSE TO VACCINATION RESPONDERS/NON RESPONDERS (%)	47/15 (75,8/24,2)	49/3 (94,2/5,8)
ANTIBODY TITER (AU/mL) MEDIAN (RANGE)	6576 (0-77673)	4023 (1.3-104689)
HEMATOLOGICAL DISEASE (N)	AML (38), ALL (5), SAA (4), CML (3), MDS (3), NHL (3), MM (2), CMML (1), MF (1), CLL (1), HL (1)	MM (26) NHL (19) HL (7)
DISEASE STATUS AT VACCINATION: ACTIVE DISEASE/COMPLETE REMISSION	1/61	9/43
G1/G2/G3	14/23/25	5/29/18
CONDITIONING REGIMEN	47 MAC/15 RIC	26 MEL 23 FEAM 2 BEAM 1 TEAM
HSCT TYPE	SIBLING/MUD/HAPLO 28/31/3	SINGLE/DOUBLE (MM) 34/18
DONOR SEX M/F	39/23	NA
DONOR MEDIAN AGE (RANGE)	34 (16-62)	NA
a-GVHD/c-GVHD	22/17	NA

TABLE 1: Patients' and healthy controls' characteristics; M: male; F: female; ALLO-HSCT: allogeneic hematopoietic stem cell transplantation; AUTO-HSCT: autologous hematopoietic stem cell transplantation; AML: acute myeloid leukemia; ALL: acute lymphoblastic leukemia; SAA: severe aplastic anemia; CML: chronic myeloid leukemia; MDS: myelodysplastic syndrome; NHL: non-Hodgkin lymphoma; MM: multiple myeloma; CMML: chronic myelomonocytic leukemia; MF: myelofibrosis; CLL: chronic lymphocytic leukemia; HL: Hodgkin's lymphoma; G1: Group 1 (vaccination within 1 year after transplantation); G2: Group 2 (vaccination between 1 to 5 years after transplantation); G3: Group 3 (vaccination more than 5 years after transplantation); MAC: myeloablative conditioning; RIC: reduced intensity conditioning; MEL: melphalan, FEAM: fotemustine, etoposide, cytarabine, melphalan; BEAM: carmustine, etoposide, cytarabine, melphalan; TEAM: thiotepa, etoposide, cytarabine, melphalan; MUD: matched unrelated donor; HAPLO: haploidentical donor; a-GVHD: acute graft versus host disease; c-GVHD: chronic graft versus host disease.

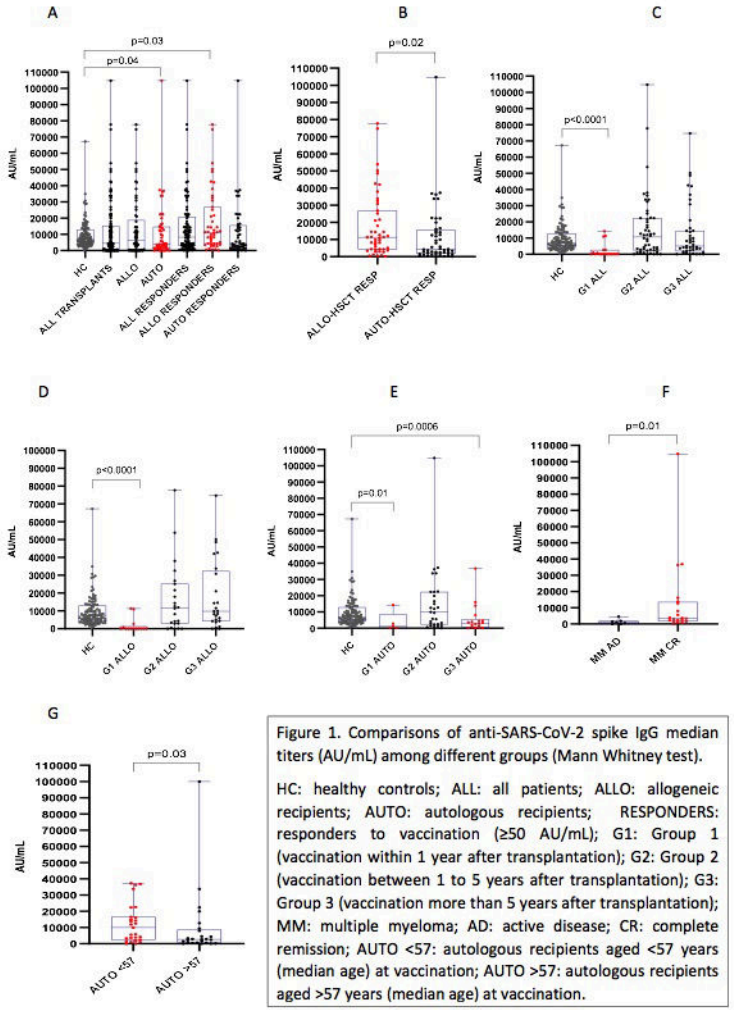

Figure 1. Comparisons of anti-SARS-CoV-2 spike IgG median titers (AU/mL) among different groups (Mann Whitney test).

HC: healthy controls; ALL: all patients; ALLO: allogeneic recipients; AUTO: autologous recipients; RESPONDERS: responders to vaccination (≥50 AU/mL); G1: Group 1 (vaccination within 1 year after transplantation); G2: Group 2 (vaccination between 1 to 5 years after transplantation); G3: Group 3 (vaccination more than 5 years after transplantation); MM: multiple myeloma; AD: active disease; CR: complete remission; AUTO <57: autologous recipients aged <57 years (median age) at vaccination; AUTO >57: autologous recipients aged >57 years (median age) at vaccination.

Figure 1